THE

VETERINARY JOURNAL

NOVEMBER, 1914.

Editorial.

THE ARMY VETERINARY CORPS AT THE FRONT.

EVERYBODY, whether in the Service or out of it, has his thoughts turned to the war and to those who are actively engaged in the present struggle against military despotism. The Army Veterinary Corps is playing its part, and that part is one of no inconsiderable importance, for the work done by the cavalry of either side has shown the necessity for the efficiency of this branch of the Service to be just as great in this, the most terrible war which the world has ever known, as it was in the battles of a century ago.

Aeroplanes, motor-cars, and all other forms of reconnaissance and transit are each very much to the front to-day, but the cavalry soldier is still with us, and no one knows better than he that his very existence depends upon the condition of his "mount." To keep his horses "fit" and to obtain the maximum use out of a cavalry unit the Veterinary Officer of the present day, up-to-date, scientific, and yet practical, with his modern ideas sensibly and usefully applied, is as essential to the other portions of a great army as the engineer officer, the commissariat department, the medical, or any branches of the whole machine which unite together to form the offensive or defensive armament of a country.

That the Army Veterinary Corps has again "justified its existence" is acknowledged on every hand, and in a recent editorial on the subject in the *Times* attention is drawn to the good work which it is doing in the veterinary hospitals and in the field.

It is stated that the horses in particular "are the admiration of everyone," and that "no doubt the excellent condition of the animals is in large measure due to the services rendered by the Army Veterinary Corps," whilst in a later paragraph, after alluding to the thousands of horses which are saved and rendered useful again, the writer goes on to say that "the work of the Army Veterinary Corps may have a very important bearing on the

campaign," as "chargers are not made in a day," and that "any horse which can be saved now by our Army Veterinary Corps may be worth six later on."

We have our great chance as a professional unit of the Army to "justify our existence," and the country has only to look at the manner in which our men have voluntarily come forward to know that we, as a profession, are as anxious as every other body of Britishers to do our share in defending the civilization and liberties of Western Europe from the disciples of Treitschke and von Bernhardi.

AN APPEAL FOR ACTIVE SERVICE NEWS.

EVERY officer, no matter to what department he may belong, is supposed to keep a "War Diary," and to the readers of THE VETERINARY JOURNAL, whether called up on duty or not, an interchange of ideas will be most instructive reading.

There are few, indeed, connected in any way with the Army Veterinary Service who could not give suggestions or furnish scientific records which would be of the utmost profit for future practice and substantially advance our methods of treating the animal to whose welfare we devote so much of our professional service. The civilian veterinary surgeon who attends the horses of a regiment in his district and sees for the first time the difference between the treatment of his patients in out-door sick lines and warm comfortable stables will be able to learn therefrom much of the utmost importance to record for our future guidance. The whole-time Territorial Veterinary Officer in Great Britain, who is similarly placed but who is able to be with his patients all day, will be able to think out and suggest improvised methods which he would scarcely have thought possible under ordinary circumstances and which will certainly be of importance and interest to others similarly placed. And the veterinary officer who is on foreign service, either in a modern up-to-date hospital of the base, a field hospital, or perhaps attached to a regiment actually in the firing line, can afford us news and scientific records of the utmost value.

To each of these sections of the profession we appeal for such information and records, however roughly compiled. We shall be most happy to do all necessary editing and most cordially to afford them the hospitality of our pages.

General Articles.

STUDIES IN THE IMMUNITY TO TUBERCULAR DISEASE.*

I.—The Caseation of the Tissues.

By CHARLES C. TWORT, M.D.Aberdeen.
Beit Memorial Fellow.

An important factor in tubercular disease is the caseation of the tissues, and the most prominent difference between this disease and leprosy is the absence, in most cases, of caseation in the latter. The question as to why the tissues caseate in some of these diseases and not in others, and why in such a disease as leprosy in the late stages of the infection caseation may sometimes be found, are of extreme interest in considering the immunity in these diseases.

According to Koch's classical hypothesis, on inoculation of tuberculin into a tubercular patient, the result of the reaction obtained is a dissolution of the tubercular tissue, which renders this site unsuitable for the further development of the specific bacillus. Thus it was considered that tuberculin acted against the tissues and not against the bacilli, and the destruction of the tissues led to death of the bacilli. This is a feasible conception if tuberculin is considered as a toxin *per se;* but at the present time it is not believed that the essence of the tuberculin reaction is due to the primary toxic effect of the tuberculin, but that an opposite state of affairs exists to that above described. From the results of my own work on acid-fast bacilli it would appear rather that it is not the soluble toxin of the tubercle bacillus which leads to caseation of the tissues, and this in turn to death of the bacilli; but, on the contrary, that the bacilli are killed by the cells and fluids of the host, and the dissolving of the bacilli and the subsequent diffusion of the endotoxins leads to death of the surrounding cells. [1]

If we consider the state of affairs in such diseases as Johne's disease and leprosy we find that the number of causative bacilli present is enormous, while caseation is absent; on the other

* From the Laboratories of the Brown Institution, University of London.

hand, in tuberculosis the number of bacilli may be scanty, with a generalized caseation of the tissues. It may be objected that, although caseation never occurs in pseudo-tuberculous enteritis (Johne's disease), it does occur in leprosy, both of man and rats. I do not deny that a slight degree of true caseation may take place in leprosy, as, for example, when the bacilli are for some reason killed by an influence but rarely present in this disease, or in old slowly growing encapsulated nodules, but the tissue necrosis found in leprosy is usually of quite a different nature. If the purulent discharge from an uncontaminated leprous lesion be examined microscopically, or still better, if a broken-down abscess in a rat be examined in the same way, it will usually be seen that the material consists almost entirely of bacilli together with a little cell *débris* and a few well-formed cells full of bacilli. There is but little granular material similar to that found in a tuberculous caseous mass, and it is evident that the liquefaction of the tissues in leprosy is simply due to the fact that it has all been utilized as food, and nothing left to act as a framework for the support of the bacilli and cells. It is significant that the few intact cells that remain appear to be quite normal, while in the centre of a tubercular caseous mass no single intact cell is demonstrable.

What are the conditions that govern the caseation of the tissues in these diseases, and why do we find this strikingly different state of affairs? Is it because the lepra and pseudo-tuberculous bacilli secrete no soluble toxins and thus do not injure the surrounding cells, and consequently escape distraction themselves, or is it because they are naturally more resistant to the fluids of the host, and in the absence of a wholesale destruction of the bacilli the tissues remain unaffected? Although I am of the opinion that no soluble toxins are secreted by these two varieties of bacilli, I believe the second factor to be the more important in relation to the absence of caseation, which view I consider to be supported by the fact that the inoculation of dead acid-fast bacilli of whatever variety invariably leads to caseation of the tissues. I have inoculated a large number of animals with Johne and lepra bacilli, and have found caseation almost always to be absent when using living bacilli, while it is invariably present on the injection of dead bacilli. In those cases in which caseation has occurred with the former the animal was

either immune to the bacillus or some other factor had influenced the humours of the inoculated animal in such a way as to cause death of the bacilli soon after inoculation. I have performed experiments which bear upon this subject, and which showed that on the inoculation of a series of normal animals with rising doses of an acid-fast bacillary vaccine a certain number of the animals will show caseous abscesses at the site of inoculation, while the skin of others remains absolutely clean, even after six injections. Rabbits inoculated intraperitoneally with an emulsion of Johne's bacillus will sometimes show large caseous masses in the abdominal cavity, while in others, under exactly similar conditions, the whole of the peritoneal membranes are quite clean. However, in discussing this question I am considering only those animals that have undergone a single inoculation, as a second injection of living bacilli will usually cause caseation. In the second inoculation the bacilli have to withstand the influence of the anticorps that are produced against the primary inoculation, and if they succumb to these anticorps then caseation of the tissues occurs as a result. It does not generally happen that all the bacilli of the second injection are at once killed out; it is only a certain number that are unable to survive, and these are sufficient to lead to intoxication of the surrounding tissues.

In some animals that are peculiarly resistant to Johne's disease, such as guinea-pigs, caseation is very frequently found in the peritoneal cavity after a single intra-abdominal inoculation, and when the contents of these caseous masses are tested on culture media they are invariably found to be sterile. It may be taken as a general rule that in caseous tissue a large number at least of the bacilli seen on microscopical examination are dead, and if no bacilli at all are found it may be safely assumed that those originally present have been destroyed and already dissolved. It is interesting to note that in general paralysis of the insane there are usually not many spirochætes in the degenerated tissue, but they are found in greater numbers in the neighbourhood of the latter. Here it is quite possible that it is the death and disintegration of the spirochætes that has led to degeneration of the tissues in which they were present.

In such affections as leprosy and pseudo-tuberculous enteritis, even in a caseous mass, the number of bacilli present is usually enormous; in fact, whether in caseous or apparently normal tissue

these two varieties of bacilli are almost always very abundant. The probable explanation of this lies in the fact that they are peculiarly resistant to lysis, for when heated emulsions are inoculated into animals it is found that Johne's bacillus can be demonstrated long after the tubercle bacillus has entirely disappeared.

It must be remembered that it is not in a single species of animal, but in all animals, whatever be their susceptibility to the tubercle bacillus, that caseation is found, while as a rule in all animals inoculated with Johne's bacillus caseation is absent. There is, however, an exception to the latter statement, for in the experimental inoculation of guinea-pigs caseation is often found, and this appears to be just the variety of animal insusceptible to Johne's disease, at any rate when intra-abdominal inoculation is resorted to.

Cattle, sheep, goats, deer, rabbits, rats, and mice have all shown themselves to be susceptible to the inoculation of Johne's bacillus, and produce evidence of the typical disease, without caseation, after varying periods of incubation. I have not inoculated guinea-pigs intravenously, but on intraperitoneal injection they do not contract the disease, and all that is seen on *post-mortem* examination are the caseous abdominal masses. Also up to the present time I have been unable to produce the typical disease in rabbits on intraperitoneal inoculation, the most I have obtained being the presence of a single bacillus in the region of the sacculus rotundus in one animal, and here again caseation of the tissues is frequently found. Among about fifty mice and rats inoculated in the same way I have never once seen caseation, and the animals frequently show definite histological signs of typical Johne's disease on *post-mortem* examination. In these fifty animals only eleven have contracted the disease, and it may naturally be asked, Why was there no caseation in the remaining animals? The reason for this is obviously because the bacilli have not been killed by the host, but have been mechanically excreted, and, as a matter of fact, I believe that the majority of these animals would eventually take the disease, as I have been able to recover the bacilli in pure culture from the thoracic and abdominal glands in practically every case. However, some of my mice had been inoculated for over a year without contracting the disease.

When rabbits are inoculated subcutaneously with *Bacillus phlei* it is especially the lungs that eventually become the seat of disease, and here one finds a caseating pneumonia with large abscesses, in fact a picture more or less identical with that found in tubercular lung disease.

On intravenous inoculation it has been shown [2] that the bacilli are excreted wholesale by the kidneys, but during the process of excretion the bacilli multiply rapidly in these organs and excite an intense leucocytic invasion. In this situation there is naturally a certain amount of destruction of the cells due to the mechanical pressure exerted by the invading bacilli and cells; but true caseation is always absent, the bacilli being gradually filtered out living, and the absorption of the lymphocytes following closely on the excretion of the agent that excites their invasion.

Again, in my experiments on the immunization of rabbits to Johne's bacillus by the inoculation of material other than acid-fast bacilli or their products, I have shown [1] that if the animal be highly immune, then on the injection of Johne's bacillus the animal collapses and dies owing to the intoxication by the products resulting from the wholesale destruction of the injected bacilli. If the animal be only partially immune, it does not die as a result of the injection of the bacilli, but if it be killed about a month later the peritoneal membrane is found to be covered with caseous masses, and, although from these masses a few isolated colonies may be obtained, it is evident from the number of bacilli seen histologically that the vast majority of them are dead. As we have seen, many normal animals may react in a way similar to these partially immune animals.

When inoculating animals with the object of obtaining the production of complement-deviating and other anticorps, I have observed that as a general rule, at least with the acid-fast group of bacilli, the inoculation of an emulsion of dead bacilli was instrumental in leading to the production of a far greater amount of anticorps than the inoculation of an emulsion of living bacilli.

Besredka and Jupille [3] observed that during the course of tubercular disease in rabbits a positive complement-fixation reaction was obtained, before microscopical lesions were evident in the organs. These authors found that the reaction ran parallel with the resistance of the animal, and the more resistant the

animal was for the injection the more intense and durable was the reaction. Thus, when inoculated with human tubercle bacilli, far better reactions were obtained than when using the bovine type. The probable reason for this is really that the inoculation of the human tubercle bacilli, very little virulent for rabbits, is more or less equivalent to the inoculation of dead bacilli, and from the above it will be seen that this should lead to the more easy production of a complement-fixing antibody than the inoculation of living virulent bacilli. It is obvious from this that the more resistant the animal the larger will be the amount of this particular anticorps produced.

Bang and Andersen [4] found that complement-deviating anticorps were more easily produced by rabbits, when they inoculated dead bacilli, than when they used a virulent strain. When the bacillus is dead the enveloping membrane probably becomes so altered that the passage of soluble material from within and without is greatly facilitated; thus the leucocytic ferments should enter, and the bacterial ferments escape more easily than in a living bacillus.

Lebedeff [5], by drying yeast and macerating it for two hours at 35° C., obtained a filtrate very rich in zymase, and thus the old method of pressure (Buchner) can be done away with. The drying is undoubtedly an important part of this process in allowing the ferment to traverse the wall of the cell, in the same way that dried acid-fast bacilli are preferable to moist bacilli for incorporating in Twort and Ingram's medium. In the animal body the bacilli, of course, never become dry, but disregarding this they will be fermented more quickly than living bacilli on account of the facility with which the specific ferment traverses the wall of the micro-organism.

The fact that in tubercular disease caseation and an intermittent temperature are predominant features, while the number of bacilli present is relatively small, and on the other hand in leprosy and pseudo-tuberculous enteritis an opposite state of affairs exists, in my opinion shows that there is a close relation between these different factors. In other words, as already mentioned, caseation, and a consequent rise of temperature, is only obtained at the expense of the death of the bacilli. This suggests a useful means for studying the effect of curative vaccines to leprosy and pseudo-tuberculous enteritis, and in-

directly to tuberculosis, for if the vaccines favourably influence the curing of the disease by directly or indirectly attacking the bacilli, which after all is the essence of a specific cure, then caseation of the tissues in the two first-mentioned diseases should become evidence, and one would be assured that the vaccine had, at any rate, a destructive action on the bacilli; and it would be reasonable to assume that properly administered it would have a beneficial effect on the patient. It is with the object of producing this caseation that I am at present engaged in studying certain non-acid-fast bacillary vaccines on rat leprosy and Johne's disease of cattle.

As Marchoux has pointed out [6], the results upon which numerous workers base the virulence of certain of their cultures, &c., of acid-fast bacilli, and the arguments that they use for maintaining the pathogenicity of the said bacilli for animals, should really be interpreted in an exactly opposite sense to that in which these authors are usually found to interpret them.

If the inoculation of an emulsion of a culture of one of the so-called leprosy bacilli produces caseation of the tissues, then, in my opinion, it proves that either it is not the true leprosy bacillus, or if it is, then it is not pathogenic for the animal inoculated. The same may be said of the marked complement-deviation reactions obtained in these animals. If the reaction is strongly positive then it is highly probable that the bacilli have been killed out soon after injection, for, as already mentioned, I have found that the inoculation of dead bacilli more readily leads to the production of complement-deviating anticorps than do living bacilli, results which are in accordance with those of Bang and Andersen, and which agree also with those obtained by Wassermann, &c., in their original experiments—I refer here to the experiments which have shown that it is far easier to demonstrate these anticorps in a patient who has undergone a course of tuberculin treatment than in those uninoculated with the specific remedy.

In conclusion, a short *résumé* may be given of what takes place in the presence of the tubercle or other bacilli producing caseation, and, on the other hand, what takes place in the presence of Johne's bacillus.

In the case of the tubercle bacillus, the soluble toxin secreted

does not probably act detrimentally on the surrounding cells, but may even act as a stimulant, so that phagocytosis of the bacilli is in no way interfered with. This toxin may have an influence in causing encapsulation of the diseased area, and thus more or less isolation from the other tissues of the body. Meanwhile the bacilli, both intra- and extra-cellular, but especially the former, commence to be disintegrated by the humours of the host. The products of this disintegration lead to a further fabrication of the specific lysin, while at the same time, if it becomes too great in amount, the animal cells are unable to survive, as the intermediate products of the breaking down of proteids are intensely toxic for the cells of the animal body. The increase of the specific lysin leads to further destruction of the bacilli, and this in turn to the liberation of more endotoxins, so that ultimately the cells inside the nodule are doomed to destruction. Thus the cells and bacilli within the constricted area react upon one another, and both in the end are killed out, the edges of the nodule, where the accumulated toxins can more easily be got rid of, being the only situation in which intact cells and bacilli can be found. Bacilli, apparently normal, may be found in the centre of the caseous mass, but rarely any intact cells; and it is quite probable that many of the bacilli here found are really dead.

In Johne's disease it is highly probable that little or no soluble toxins are produced, and the bacilli, although actively phagocytosed, are not toxic for the cells, and can live and multiply within them. At the same time, if a certain number of bacilli die or are killed by the host, the products of disintegration are better able to get away than in tubercular disease, as the lesions are never encapsulated, but blend more or less imperceptibly with the normal tissues In leprosy the lesions are often encapsulated, but here again it is probably due to the non-toxicity of the bacilli for the cells, and especially on their ability to live and multiply within the cells, that there is an absence of caseation. The disintegration products of Johne's bacillus and the leprosy bacilli are as toxic for the animal as a whole, or locally for its tissues, as those of the tubercle bacillus, which is seen by the reaction produced on inoculation of a diagnostic vaccine on the one hand, and the effect produced by the inoculation of an emulsion of dead bacilli on the other, when with all three diseases, and with all three bacilli, the results are the same, that is to say, a rise of

temperature in the first case and caseation of the tissues in the second.

[1] TWORT, C. C.: "The Immunity to Tubercular Disease and Diseases caused by Micro-organisms allied to the Tubercle Bacillus," Thesis, Aberdeen, February, 1914.
[2] TWORT, C. C., and CRAIG, T.: "The Pathogenicity of Johne's Bacillus compared with that of Other Acid-fast Bacilli for some of the Laboratory Animals." *Central. f. Bakt.*, 1913, Bd. 68, p. 455.
[3] BESREDKA et JUPILLE, *C. R. Soc. de Biologie*, February 14, 1914.
[4] BANG, O., und ANDERSEN, C. W.: "Einige Untersuchungen über Komplementbindende Antistoffe, &c.," *Central. f. Bakt.*, 1913, Bd. 69, Heft 7.
[5] LEBEDEFF: "Extraction de la zymase par simple maceration," *Ann. de l'Institut Pasteur*, 1913.
[6] MARCHOUX: "La lèpre du rat," *La Presse Médicale*, 1914, No. 22.

FURTHER INVESTIGATIONS INTO THE ETIOLOGY OF WORM NESTS IN CATTLE, DUE TO *ONCOCERCA GIBSONI*. By J. BURTON CLELAND, M.D., CH.M.

[Abstracted by A. W. N. P.]

IN a pamphlet of some 60 pp. Dr. Cleland gives an account of experiments and observations which have been carried out since the 1911 report of the Bureau. The details of this report were published in the veterinary Press at that time on account of the interest taken in worm nests during the inspection of imported meat. Although the present work only deals with the biology of worm nests in cattle, it must be remembered that *Oncocera* species also occur in man, the horse, and other ruminants. It is therefore likely that experiments and observations which either negate our previous views or add new ones, will be of great value to helminthology in general. The report as now submitted adds considerably to our knowledge of the subject and seems to reduce within a narrow compass the question of the means of conveyance of the disease.

PART I.—GENERAL.

(Abstract). There is a short account of the prevailing view with regard to the transmission of these worms from ox to ox, and it is stated that although the actual conveyer of the disease has not been determined, most of the evidence favours the view that *Stomoxys calcitrans* is the culprit. The more important results that have been obtained may be summarized as follows:—

(1) Various Muscidæ as well as mosquitoes can ingest the embryos of *Oncocerca gibsoni* when given access to a freshly-opened nodule.

(2) In the case of *Stomoxys calcitrans* not only can the embryos be ingested but they may remain alive and active and in considerable numbers within the alimentary canal in this insect for a period of three days at least. They have not, however, been detected alive after a longer period.

(3) In the case of *Musca domestica* and *Musca vetutissima*, both common flies, we find that the embryos can be ingested, but that in the few experiments so far conducted they have not been found alive in the alimentary canal of these insects, even twenty-four hours after feeding.

(4) Embryos of *Oncocerca gibsoni* have been found in a small thickened area in the skin of the belly of a calf. This area contained no adult worm, and at the *post-mortem* examination later it was found to be far separated from any worm nodules. Probably quite twenty or thirty embryos were present in this small area. By teasing a fresh preparation they were found alive and at various depths below the surface epithelium, sometimes in a fibrous stroma, sometimes near the root sheaths of hairs. In this situation they were often intricately curled, though sometimes they were in looser loops. Their depth below the surface was in many instances much less than the length of the proboscis of *Stomoxys calcitrans*.

(5) Another similar area in front of the shoulder of a cow was pricked and in the exuding juice an embryo worm was detected.

(6) A calf, which had been born on the island, was later killed, and most of the worm nests were found in a state of degeneration. One or two, however, still contained living embryos. A single embryo was detected in the subcutaneous tissue of the front of the left foreleg by means of a smear made at the *post-mortem* examination.

(7) Two bulls, which were under experiment at Milson Island, both showed at the *post-mortem* examination numerous worm nodules. In one case these were exceedingly numerous, amounting to at least 135. The nodules were all comparatively small and only a few were degenerated. They contained, in the several instances in which they were examined in a fresh state, active embryos. These animals came from parts of the State in

which worm nests are not considered to be present or, at least, prevalent. Their duration at Milson Island was in each case a little longer than a year. Everything points to their having been thus heavily infected at Milson Island itself. The distribution of these animals on the island, moreover, supports the view that infection had taken place by means of a biting and flying insect.

(8) In one of these bulls a number of embryos were found in smears made from various cutaneous situations. In the other, embryos were found in one subcutaneous situation (the brisket). In a calf, an embryo was found in a smear from the front of the right shoulder. In a cow, an embryo was found in the subcutaneous tissues of the left fore fetlock, and another in a similar situation from the outer aspect of the right stifle. It will thus be seen that in no less than six animals embryos were met with in subcutaneous situations apart from worm nests, in two instances during life, in five instances (out of seven animals in which particular search was made) at the *post mortem*.

(9) An *Oncocera* about 9 in. long was found in the loose tissues of the back part of the knee-joint in a bull. This worm was not encapsuled though a small fibrous nodule was attached to part of it.

(10) In one instance a group of two female worms containing living embryos and two males was found loosely coiled near the hip joint. These worms were not surrounded by any increase of fibrous tissue, but portion of another was found embedded in a small lymphatic gland.

(11) The portion of a worm embedded in the small gland showed a diameter unquestionably less than the smallest part of an adult male removed from its neighbourhood. This indicates that this particular worm was less developed than its free neighbours. That it had been in this situation in the lymph gland for some considerable time is evidenced by the presence of giant cells surrounding it. It may be thrown out as a suggestion worth further consideration, that perhaps an early stage of the worm is passed in the lymphatic glands, the embryos reaching these soon after inoculation to the bovine host. After developing to a certain extent the worm may then escape and develop further whilst wandering through the tissues, this particular worm found in sections of the lymph gland being considered as having undergone a pathological arrest. An interesting series of speculations

XUM

are raised by this finding when we consider the relationship of *Filaria bancrofti* of man to the lymphatic glands of the groin and other areas, and the occurrence of elephantiasis.

Suggested Life History of *Oncocerca gibsoni.*

From the data accumulated, more especially the recent findings mentioned later in this paper, the following seems to me to be the probable life history of *Oncocera gibsoni.*

By means of a biting insect, either *Stomoxys calcitrans* or *Culicelsa vigilax*, embryos are ingested from the bovine host. In the insect a certain stage of development takes place, and eventually the partly developed worm or worms are injected into the subcutaneus tissue of the new bovine host. Having reached the subcutaneous tissue, the young worms start on the migrations, and incidentally increase in size. Probably their own active movements combined with the muscular contractions of the host and the onward flow of lymph, determine a progressively upward movement from the lower parts of the limbs (if there injected) towards the body. Thus, if the worms were injected into the lower parts of the hind legs, they would tend to work upwards past the stifles and round the side of the body towards the front of the belly. Here they could pass under the various muscular planes, which would account for their presence beneath or between the oblique muscles and the muscular masses entering the brisket. From the fore limbs they might similarly reach the brisket area. That the worms are intended to migrate through the tissues, and that such migration is of value in the perpetuation of the species, is, I think, evidenced by the spiral rings which pass round the body, and which are obviously of assistance in preventing the animal, after it has moved forward, from being forced back again. When for some reason or other the adult worm gets arrested—and probably during its wanderings it is more likely to be arrested in some situations, for example, the brisket, than in others—then the embryos which still continue to be liberated produce a reaction in the surrounding tissues, so that eventually the worm becomes encapsuled in a dense fibrous mass which increases in size as time goes on. The embryos themselves may appear in the tissues in one or two ways, either having been deposited during the migrations of encapsuled worms or after having escaped from a developing worm nest before its capsule

has become too dense. In the former instance the young worms may be deposited in situations where biting insects have easy access to them, whilst in the other the active movements of the embryos would probably eventually lead to a certain number of them occupying suitable positions for ingestion by insect hosts. It is possible that even in an early stage the slight difference in size noted represents the difference in sex. The life cycle would be completed by the ingestion of these embryos from the subcutaneous tissues by the intermediate host, and it is probable, if migrating worms are the source of most of the embryos in the skin, that several embryos might frequently be ingested at the one time.

PART II.—SPECIAL INVESTIGATIONS AND EXPERIMENTS.

Detailed accounts are given of experiments with *Stomoxys calcitrans*, to test the length of life of ingested embryos in it, and to infect a calf by means of it. The inoculation and ingestion of the embryos were also tried upon calves. Lice were also experimented with.

PART III.—EXAMINATION OF CATTLE ON MILSON ISLAND, NATURALLY INFECTED WITH WORM NESTS.

The results of fifteen *post-mortem* examinations are recorded, and tables are given to show the number of worm nests encountered, their size, situation, and condition, together with the presence or absence of active embryos.

A series of photo-micrographs of the worms and embryos *in situ* concludes the work.

TETANUS: ITS PREVENTION AND TREATMENT BY MEANS OF ANTITETANIC SERUM.*

BY ALFRED MACCONKEY, M.B., B.C.CANTAB., D.P.H.

Bacteriologist in Charge of Serum Laboratories, Lister Institute of Preventive Medicine.

TETANUS cannot be said to be of frequent occurrence under ordinary conditions of life in time of peace, but the outbreak of war is often followed by a comparatively large increase in the number of cases of this disease.

---

* Reproduced by the courtesy of the Editor of the *British Medical Journal*.

These notes, the fruit of work in a serum laboratory and of a slight cultivation of the literature, were gathered together some months ago without any idea of their appearing in their present form, and I now publish them with the object of calling the attention of those who have not specially studied the question to the value of tetanus antitoxin, which is inestimable when the serum is used properly as a prophylactic. It is to be hoped that at the present time systematic use will be made of this remedy, so that one, at any rate, of the hazards run by those who are offering their all on the battlefield in defence of their country may be reduced to a minimum.

Historical.

Tetanus, or lockjaw, is a malady common to man and many animals. It was recognized in ancient times, and it has long been known that it was likely to follow the soiling of wounds with earth, dust, and similar material. About the middle of the nineteenth century the impression gained ground that it was due to the production of a poison in the wound, and in 1884 Carle and Rattone reported that they had conveyed the disease by means of pus from a case of tetanus.

In 1885 Nicolaier produced tetanus in mice, guinea-pigs, and rabbits by inoculating them with garden soil, and the pus from the wounds carried on the infection from animal to animal. In the local lesion Nicolaier found a bacillus with a spore at the end, but he did not succeed in obtaining a pure culture.

In 1886 Rosenbach found a similar bacillus in a case of human tetanus, but he also was unsuccessful in his attempts to isolate it. Knut Faber (1889) separated the toxin from mixed cultures by means of filtration through porcelain. Kitasato in 1889 was the first who succeeded in securing a pure culture of this bacillus and in proving that it alone was the causal agent of the disease.

Distribution of the Bacillus.

The *Bacillus tetani* is widely distributed in nature, being found in the soil of most cultivated areas, in the streets of cities, and, in fact, in any place where there is fæcal contamination. v. Lingelsheim recalls the examination by Bossano of samples of dust from thirty-eight towns, only twelve of which were found

free from tetanus bacilli. Nicolaier found it in twelve out of eighteen samples of earth in the neighbourhood of Göttingen.

Choukévitch (1911) demonstrated its presence in the intestinal contents of two horses out of eighteen, but Lukas (1914) was more successful, as he isolated it from the fæces of sixteen out of seventeen horses. Joseph (1910) examined the excreta of cattle, and came to the conclusion that the *B. tetani* must be considered a normal inhabitant of the intestine of these animals. Römer (1909) also found it frequently in the fæces of adult cattle, but it was not usually present in animals under 2 years of age. Further, tetanus antitoxin was found in the blood of the older animals in more than 50 per cent. of the cases examined. Dolly (1910) found tetanus bacilli frequently in the wads of blank cartridges, and Graser (1910) reports a like result. Rabinowitsch (1907) found the spores of this bacillus in the water in which strawberries sold in Berlin had been washed. It is said to have been found in the mud of the Dead Sea.

This wide distribution of the organism emphasizes the necessity for extreme care in cleansing all wounds, but especially those which have come in contact with street dust, road sweepings, the soil of cultivated fields, garden earth, manure, &c.

Bahnson (cited by Anders and Morgan) stated that during the American Civil War he was put with other prisoners into a shelter that had been used for horses, and that all the wounded placed there who did not die as a direct result of their wounds developed tetanus, and all of them died.

Cultivation of the Bacillus.

Under the usual conditions of artificial cultivation in pure culture the tetanus bacillus will not grow in the presence of oxygen, and therefore it is termed an "anaerobic" organism. But if some nutrient medium be inoculated with the *B. tetani*, and also with some oxygen-loving organism, such as the *B. subtilis* (hay bacillus), the absence of oxygen is not so necessary, as the *B. subtilis* will use up the oxygen and produce conditions in which the *B. tetani* can grow. Further, Tarozzi and others have shown that if pieces of animal tissue be placed in a liquid culture medium the bacilli will grow alone in the presence of oxygen, the dead tissue acting as a reducing agent.

In nature we get a combination of these two methods of

producing conditions suitable for growth; in the earth we have organic materials to act as reducing agents and the aerobic organisms to use up oxygen; in contused and dirtied wounds we have the dead tissues and the pyogenic cocci to act in a similar manner.

Production of Tetanus Toxin.

Tetanus toxin is prepared by growing the tetanus bacillus in nutrient bouillon, of neutral or slightly alkaline reaction, which may or may not contain some reducing agent, such as glucose, sodium sulphindigotate, &c. Special flasks filled with such a broth are inoculated with the tetanus bacillus, hydrogen gas is passed through the liquid, and the flasks are placed at 37° C. for eight to ten days, when the bouillon is filtered through porcelain to remove the bacilli and spores. The filtrate forms the tetanus toxin. The toxicity of such a filtrate varies very much. A mouse of 15 grammes weight might be killed in three to four days by $\frac{1}{5000}$ c.c., or it might be necessary to inject $\frac{1}{1000}$ c.c. or even more. The susceptibility of different species of animals to this toxin varies very markedly; thus it is stated that if a certain quantity of toxin will just kill 1 gramme of mouse the same quantity will kill

6 grammes	of guinea-pig	$\frac{1}{5000}$ gramme	of cat
12 ,,	horse	$\frac{1}{1000}$,,	goose
$\frac{1}{2}$ gramme	of goat	$\frac{1}{4000}$,,	pigeon
$\frac{1}{150}$,,	rabbit	$\frac{1}{3000}$,,	hen

from which it is evident that the horse is one of the most susceptible of animals.

Production of Tetanus Antitoxin.

In 1890 Behring and Kitasato showed that animals could be immunized against the tetanus bacillus and its toxin, and that then their blood had acquired a new property, so that when it was injected in suitable quantity into other animals these were protected against doses of tetanus which otherwise would be invariably fatal. This new property, they thought, was due to the development in the blood of immunized animals of a substance which, as it neutralized the toxin, they called "antitoxin." When the fluid part of the blood has been separated from the solids it is found that the antitoxin is contained in the plasma or serum. Horses are the animals most frequently used

in the production of tetanus antitoxin for therapeutic purposes. As they are so highly susceptible to the toxin, the utmost care is required during the process of immunization to avoid the occurrence of accidents. Therefore, at the beginning of the immunization the toxin is not given in the pure state, but only after having been modified by chemicals or by being mixed with antitoxin. Sometimes the toxin and the antitoxin are not mixed, but are given simultaneously in separate parts of the body, or the antitoxin is given a few hours before the toxin. Whichever method is used at the commencement the object is always the same, namely, to produce a basal immunity so that after a time the animal will bear without ill-effect the inoculation of pure toxin. Therefore, as the injections are repeated the amount of modifying agent is gradually decreased until only the toxin is given. When the establishment of a basal immunity has been demonstrated the doses are increased more rapidly, and finally 200 c.c., 400 c.c., or 1,000 c.c. of pure toxin are injected at one time. The inoculations are usually given subcutaneously or intramuscularly (though some use the intravenous route) at intervals of five to ten days. After the final dose a rest of one to three weeks is given before the animal is bled, when on an average 8 litres of blood are withdrawn. If considered desirable another bleeding may be taken at the end of a week, and followed by a third, fourth, or fifth at intervals of seven or eight days. The animal then has a rest of three weeks or more before being reimmunized. During a bleeding, as well as during all subsequent processes, every precaution is taken to prevent contamination. When the plasma or serum has been obtained separate from the corpuscles and clot a small amount of preservative is added, and it is put away in a cool dark place for a time.

As soon as possible after a bleeding the serum is tested to ascertain whether it contains enough antitoxin to render it fit for therapeutic use. This standardization is carried out according to the American method introduced by Rosenau and Anderson (1908), a description of which has been published in *Bulletin* No. 43 of the United States Public Health and Marine Hospital Service and in the *Journal of Hygiene*, January, 1914.*

* The Lister Institute serum is thus standardized.

When required for use the serum is filtered through porcelain and distributed into small bottles. Before being sent out for therapeutic use antitetanic serum is tested:—

(1) *For absence of toxicity* by animal experiment, 10 c.c. of serum being injected subcutaneously into each of two guinea-pigs of 250 grammes weight. The animals must remain well.

(2) *For sterility* by cultural experiment aerobically and anaerobically. The media inoculated with the serum must not show any growth.

(3) *For non-excess of preservative*, 0·5 c.c. of serum being injected subcutaneously into a mouse of 15 grammes weight. The animal must not show more than temporary symptoms of intoxication.

From the time the serum is first obtained its antitoxin content begins to diminish. This diminution takes place most rapidly at first; later the serum appears to reach a condition of comparatively stable equilibrium, when the deterioration proceeds much more slowly. To compensate for this unavoidable loss there is usually put into each bottle an amount of antitoxin in excess of the quantity stated to be present, sufficient to make it probable that the bottle will, at the end of two years, contain the amount of antitoxin stated on the label, provided it is stored in a dark cool place—preferably in an ice-chest.

Prophylactic Use of Tetanus Antitoxin.

Tetanus antitoxin may be used (1) prophylactically, (2) curatively.

As a prophylactic tetanus antitoxin yields excellent results.

Animal experiment has proved:—

That if a fatal dose of tetanus toxin be mixed together with a suitable amount of tetanus antitoxin, the mixture can be injected into animals without giving rise to any ill-effect whatever.

That the effect of a fatal dose of toxin can be completely inhibited by the injection of antitoxin twenty-four hours previously.

That a fatal result can be prevented by injecting a suitable dose of serum within a short time of the injection of the toxin.

From these results it would naturally be expected that tetanus antitoxin would furnish good results when used as a prophylactic. Such has been the case.

Vaillard (1912, p. 224) refers to the practice of eight veterinary surgeons from 1898 to 1906. In that period they inoculated 13,124 animals after operations or accidental wounds, and not a single case of tetanus occurred among them. During the same time two veterinary surgeons alone saw 139 cases of tetanus among animals which did not receive the treatment. If the figures of Nocard and Labat are added, we get 16,917 animals which had a prophylactic injection, and among them one single horse had tetanus—in this case the antitoxin was given five days after the wound, and the attack was very benign.

Huguier (1909) used to give two injections of 10 c.c. each of antitetanic serum, but for some years has been content to give one, and, although he operated in conditions under which infection was most possible, he has not had one case of tetanus among horses thus treated prophylactically.

Dieudonné (1909) records 1,009 operations for castration or hernia, with no case of tetanus, although only a single injection of serum was given. During the same period he observed 87 cases of tetanus among horses operated on or wounded which had not had a prophylactic injection.

Parker Hitchens (1910) has proved experimentally that a dose of 300 U.S.A. units of tetanus antitoxin will protect a horse against an infection fatal to the control animals.

Mohler and Eichhorn (1911) found experimentally that as regards an infection fatal to the control:—

300 U.S.A. units given forty-eight hours after infection = no symptoms of tetanus.

500 U.S.A. units given seventy-two hours after infection = no symptoms of tetanus.

700 U.S.A. units given ninety-six hours after infection = no symptoms of tetanus.

Whereas—

250 U.S.A. units given forty-eight hours after infection = local tetanus. Recovery.

400 U.S.A. units given ninety-six hours after infection = local tetanus. Recovery.

They conclude "that 500 U.S.A. units is a sufficient dose of antitoxin for use as a prophylactic, even in cases where the infection has occurred four days prior to the injection of antitoxin."

The experience of veterinary surgeons is therefore all in favour of the value of the prophylactic use of antitetanic serum. The results of its use for a similar purpose in the human subject are scarcely less decisive.

Vaillard (1912) cites the experience of Biron and Pied. These surgeons did not use serum from 1895 to 1902, and had during those years eleven cases of tetanus, which were all fatal. In 1903 they began to use serum systematically in every case in which there was a chance of infection with tetanus. From 1903 to 1910 there was not a single case of tetanus in their practice, but during this period they received into their wards four cases of tetanus from outside; three cases of tetanus were taken into other wards of the same hospital, and there were two deaths from tetanus in the town. Vaillard refers also to cases of tetanus following wounds received during the celebrations on July 4 (Independence Day) in America. In 1903 there were 415 cases of tetanus. Then the prophylactic treatment was strongly urged and began to be made use of.

In 1904 there were	...	...	...	105 cases.
In 1905 ,, ,,	...	...	...	104 ,,
In 1906 ,, ,,	...	...	...	89 ,,
In 1907 ,, ,,	...	...	...	73 ,,

These figures suggest that, as the years passed and the beneficial results were recognized, more and more attention was devoted to prophylactic serum treatment.

Confirmatory evidence has also been brought forward by Brandenstein (1908); Bockenheimer (1909); Solieri (1910), thirty-five cases with one death; Graser (1910), no case of tetanus in eight years among patients treated prophylactically; Simon (1913, p. 236), citing Liell's analysis of 350 cases of Fourth of July wounds and tetanus, shows a mortality of 98 per cent.; only seven recovered, and of these five had prophylactic treatment. In 1907 the Editor of the *Journal of the American Medical Association* summed up the case as follows:—

"A fairly careful scrutiny of the American literature for the past five years has not brought to light a single report of the development of tetanus in a person who received a timely prophylactic dose of tetanus antitoxin."

We thus see that the inestimable value of tetanus antitoxin when properly used as a prophylactic is beyond question.

In connection with the words "properly used" in the previous sentence, it is important to remember that antitetanic serum is an antitoxic and not a bactericidal serum. It has no power to inhibit the growth of the bacillus. All antitoxin can do is to neutralize the toxin produced. A certain amount (x) of serum can neutralize a certain amount (y) of toxin and no more. Any further toxin produced can exercise its deleterious effect uninfluenced by the serum. Thus if an animal has been infected by tetanus and has received a prophylactic dose of serum it is protected against the toxin produced until the neutralizing power of the serum has been exhausted. When that stage is reached, then, as Vaillard puts it, if more toxin is elaborated one of three things must happen, either:—

(1) More antitoxin must be given; or

(2) The animal must produce its own antitoxin; or

(3) The animal must become intoxicated.

Further (*cf.* Tarozzi *supra*), the tetanus bacillus can multiply and produce toxin in blood-clots, or in necrotic tissue, especially in the depths of a wound; and as there is some evidence suggesting that a sharp fall may occur in the antitoxin content of the blood about one week after an injection of antitoxin, it is advisable to repeat the injections weekly as long as there is any necrotic tissue in a wound. Again, there may be necrotic tissue in a wound several days old, or a large amount of dirt may be ground into the tissue—for example, run-over cases—and it may be decided to operate and thoroughly clean up such a wound. In this case it is advisable to give a prophylactic dose of antitoxin intramuscularly some hours before the operation, as acute tetanus has occurred within twenty-four hours of such operation, and has in all probability been due to the rapid absorption, by the fresh tissues laid bare by the operation, of a large dose of tetanus toxin which had been elaborated in the necrotic tissue, or was present in the dirt with which the wound was soiled.

Dose.

The amount of serum which should be given at each injection depends entirely upon the number of units in each cubic centimetre of the serum. We have seen above that for the horse, which is the animal most susceptible to tetanus poison, the Americans have experimentally demonstrated the dose to be 300

to 500 U.S.A. units; but in the case of man we have no such evidence. v. Behring recommends 10 to 20 units. These units are German units, and one of them is equal to about 40 U.S.A. units. The dose would then be 400 to 800 U.S.A. units.

Vaillard mentions 10 c.c. as the dose for superficial easily cleaned wounds, not grossly soiled; 10 c.c. of the tetanus antitoxin sold by the Pasteur Institute usually contains from 500 to 1,000 U.S.A. units.

Tizzoni considers that 200,000 of his own units is an ordinary prophylactic dose. I have only examined one sample of Tizzoni's serum.* The bottle contained 5 c.c. = 200,000 units Tizzoni = 125 units U.S.A.

Park and Williams (p. 243) say: "It is the custom at many dispensaries in New York City and elsewhere to immunize all Fourth of July wounds by injecting 1,000 units. None of these have ever developed tetanus."

From this last statement we would conclude that 1,000 U.S.A. units is an ample prophylactic dose, as it has always prevented tetanus, and that it is quite possible a smaller dose would answer the purpose. This apparently has been found to be the case by v. Behring, Vaillard, and Tizzoni.

Where there is plenty of serum at the disposal of the surgeon there is no need to take thought about the size of the dose, and the ample dose of 1,000 to 1,500 units may be given with the knowledge that it is better to give too much than too little. But when, as may easily happen during war, there is only a limited amount of serum available, then the question of the smallest protective dose becomes important. This may be put down as about 500 U.S.A. units for a simple uncomplicated case, and as the amount of soiling of the wound and contusion of the tissues increases so should the amount of antitoxin be increased.

The interval of time between the infliction of the injury and the injection of serum also has to be taken into consideration when fixing the dose. Dönitz (1897) showed experimentally in rabbits that if an hour were allowed to elapse between the injection of the toxin and that of the serum it required forty times the neutralizing dose (*in vitro*) of serum to save the life of the animal. Studying the same question recently on guinea-

* Cf. *Journal of Hygiene*, January, 1914.

pigs I found that while $\frac{1}{10}$ U.S.A. unit of antitoxin neutralized 100 minimal lethal doses (M.L.D.) of tetanus toxin *in vitro* it required 1 unit of antitoxin to neutralize 1 M.L.D. when given subcutaneously and simultaneously, but in different parts of the body, but 3 units did not save life when given four hours after the toxin. When the serum was given twenty-four hours after 1 M.L.D. of toxin it required 2,000 units of antitoxin to save life, though even this amount did not prevent the onset of the disease. In these animals 1 M.L.D. almost always caused the appearance of slight signs of tetanus at the end of twenty-four hours after the injection of toxin.

It is obvious, then, that the earlier the prophylactic dose is given the more certain will be its effect in preventing tetanus, the smaller within limits will be the dose, and the smaller the cost of treatment. This last item may seem insignificant, and it is so when it is only a question of the prophylactic use of antitoxin; but it will be found to loom large in the picture when it is necessary to consider the value of tetanus antitoxin from a curative point of view.

Curative Use.

"*Premonitory*" *Symptoms.*—In all diseases the earlier treatment is commenced the greater the chances of a favourable result. If we could recognize tetanus in a stage as early as we can diphtheria, it would no doubt be possible to obtain just as good results from serum treatment. But tetanus, unlike diphtheria, has no characteristic lesion which appears early in the attack and gives an indication of the nature of the disease. As it has been aptly put by Dr. C. J. Martin, the diagnostic membrane in diphtheria corresponds to the dirt or other foreign body carrying the infection of tetanus, and so, just as we give diphtheria antitoxin when we see such a membrane, so ought we to give tetanus antitoxin when we see any such infecting material in a wound. When the symptoms of tetanus are distinct it means usually that the disease has made very considerable headway, and has reached that stage which in diphtheria would be looked upon by some as beyond the reach of the beneficial influence of antitoxin.

This explains to some extent the uncertain results which follow the use of antitoxin as a curative agent, and it also raises the question whether there are any "premonitory"

symptoms the presence of which might rouse a suspicion that a case was one of commencing tetanus. A study of some of the literature of tetanus has shown that commencing tetanus has been mistaken for "colds," muscular rheumatism, stiff neck, sore throat, influenza, mumps, &c., and it has even been suggested that many cases which have been diagnosed and treated successfully as cases of the above diseases have in reality been slight attacks of tetanus. With the object of directing attention to what may prove to be "premonitory symptoms," K. Evler (1910) relates thirteen cases of tetanus with two deaths, which came under his personal observation, he himself being one of them. He describes these "premonitory" symptoms as being very varied and changeable.

A day or so after the infection there may be general restlessness, changing suddenly to a desire to rest.

Sleeplessness with distressing dreams, and it may be nightly delirium.

Difficulty in micturition due to spasm of the sphincter vesicæ, which may last from a few minutes to half an hour.

Temporary giddiness, violent headache, excessive yawning.

The facial appearance changes and the patient looks anxious, though there is no risus sardonicus yet.

There may be trembling of the tongue, which is put out to one side.

There is often a profuse sweating, and darting pains in various parts may occur.

The patient may have a feeling of chilliness, and there may be some swelling, without redness locally, of the injured member and throbbing of its arteries notwithstanding that the limb is raised.

Slight jerking may follow pressure on the flexor tendons, and these muscles may be noticed to be in a condition of increased irritability.*

If symptoms such as these are present with a history of possible infection with the tetanus bacillus Evler considers that the administration of serum is justified. The later symptoms include:—

Increased flow of saliva.

* This condition of increased irritability of the flexor muscles has been noticed to occur in horses quite early in an attack of tetanus.

Reflex cramps of œsophagus.

Ocular symptoms; for example, nystagmus, strabismus.

Ear trouble, and spasmodic cough.

Tremors and clonic spasms which are not painful and which may not attract attention.

Pain persisting after muscular contraction induced by effort.

Swollen and reddened lymphatics, enlarged glands and tenderness in the infected region.

Evler infected himself during an operation, and early symptoms developed within twenty-four hours. He presented nearly all of the symptoms mentioned. Serotherapy was commenced on the fifth day. Nutrient enemata became necessary on the seventeenth and eighteenth days, but on the nineteenth the teeth could be opened a little and recovery then progressed satisfactorily.

Evler's paper directed my attention to these "premonitory" symptoms, and since reading it I have carefully read through a considerable number of cases of tetanus described in the literature, and I have found that practically all the symptoms mentioned by Evler have been noticed as being present early in the disease. All have not been observed in the same patient, but usually the one or two present have been sufficiently prominent to force themselves upon the notice of the physician, and, if he had read Evler's paper, to remind him that such a disease as tetanus might be before him.

If tetanus be studied from the standpoint of these "premonitory" symptoms there is reason to hope that as our knowledge of them increases so will our power of combating the disease be increased by our intervention earlier in an attack.

Curative Value.

The results following the use of antitoxin as a curative agent have been for the most part unsatisfactory up to the present. The reasons given to account for this are that the disease is usually diagnosed only when it has made considerable progress, and that the toxin is absorbed and travels along paths where it is beyond the influence of antitoxin.

In most cases the tetanus bacilli remain and multiply at the site of infection, and the toxin there produced is absorbed and carried to the central nervous system. As regards the path

by which it travels numerous observers have corroborated the findings of Meyer and Ransom that tetanus toxin is chiefly absorbed from the infected wound along the motor nerves of that region, and passes by direct extension into and through the spinal cord, but it may also pass into the circulation. It is also thought that in the nerves the toxin passes along the axis cylinder. Some observers, however, do not agree entirely with these conclusions.

Cernovodeanu and Henri (1907) have stated that if the vessels and muscles of a limb be tied while the nerves remain intact, a large amount of tetanus toxin may be injected without the production of tetanus, and they therefore conclude that, while some toxin is absorbed by the nerves the larger part passes along the lymphatics and blood-vessels.

Field (cited by Park and Williams) is of opinion that the toxin does not pass along the axis cylinder but along the lymphatics of the nerves.

Permin (1912-1913), from a critical analysis of the literature and from the results of a large number of experiments performed by himself, concludes that part of the toxin is taken up by the peripheral muscle nerves of the site of infection and passes along the axis cylinder to the spinal cord, and part passes into the lymph and blood and, gaining the general circulation, may pass directly to the ganglion cells of the cord or indirectly by means of the peripheral nerves.

There is, then, no unanimity of opinion as to the special road taken by the toxin, but what we know is that somehow the toxin passes along the nerves comparatively rapidly, but the amount found in the cerebrospinal fluid is not great—on several occasions 1 to 2 c.c. of this fluid have contained a fatal dose for a mouse but not more toxin than this.

The holding of the opinion that the toxin is absorbed by the nerve endings and passes along the axis cylinder—that is, in a situation which is beyond the reach of antitoxin in the blood—renders the curative treatment of declared tetanus practically hopeless, in the opinion of many clinicians. Antitoxin does not appear to penetrate readily into the substance of the peripheral nerves or of the central nervous system, and therefore all it can do is to neutralize only the toxin which has not been absorbed, or which is in the blood-stream. (After huge doses of antitoxin,

given intravenously, only traces of it can be found in the cerebro-spinal fluid.) So a cure can result from the employment of antitoxin only so long as a fatal dose of toxin has not been absorbed. Many cases are on record, and many experiments which seem to confirm this view.* The experiments of McClintock and Hutchings (1913) will serve to illustrate this point. They took sheep with long tails and inserted into the tip of the tail a splinter of wood which had been infected with tetanus spores free from toxin. The first symptoms of tetanus occurred six to eight days later, when the tail was at once amputated, 20 cm. being removed, and 4,500 U.S.A. units of tetanus antitoxin were given intravenously and repeated daily. Every animal but one died, and the symptoms did not seem to be influenced by the serum. The amount of toxin in the blood, as proved by animal experiment, was at its maximum between the fifth and seventh day—2 c.c. of blood containing a fatal dose for a guinea-pig of 350 grammes weight. No toxin was found in 2 c.c. of the blood twenty-four hours after the injection of serum.

From these results it has been concluded that as amputation of the tail had no effect upon the progress of the disease, and as there was toxin in 2 c.c. of the blood before but not twenty-four hours after the commencement of serum treatment, therefore by the time that the first signs of tetanus appeared a fatal dose of toxin either had been absorbed and fixed, or if not completely fixed was in a situation where the antitoxin could not reach it to prevent complete fixation. This being the case, all that can be expected from serum treatment is the prevention of further absorption of toxin by blocking all the paths leading from the infected area—the nerve routes by injection into the nerves of the region affected and the vascular route by large injections into a vein—and all this merely in the hope that a fatal dose of toxin has not already been absorbed.

It is not certain, however, that these views are correct. They may be based on a false premise, namely, that antitoxin must penetrate into the cell before it can neutralize the toxin attached to the cell.

---

* NOTE.—For a most excellent review of the literature of this subject, *cf.* Permin, 1913.

But the recent work of Kraus and Amiradzibi (1910) suggests that, contrary to the usual acceptation, a toxin must pass out of a poisoned cell before it can be neutralized by its antitoxin, as the latter cannot penetrate into the cell; and further, that the rate of diffusion of the toxin out of the cell is accelerated by the presence of antitoxin in the surrounding fluid.

Moreover, von Graff and Menschikoff (1912) have shown experimentally that it is possible to extract tetanus toxin from liver cells by means of antitoxin. They allowed the cells to remain in contact with a solution of toxin during one hour at 37° C. Then they removed the cells and washed them free from surrounding toxin. Some of these washed cells were injected into mice and caused tetanus. The remainder were soaked in a solution of tetanus antitoxin for one hour at 37° C., and then removed from the serum, washed free from surrounding antitoxin and injected into mice, which remained quite well. Control experiments showed that while toxin could pass into the cell and be so firmly fixed that several washings would not remove it, serum, on the other hand, could not pass into the cell in any demonstrable quantity. It is justifiable, therefore, to presume that the toxin was extracted from the cells by the surrounding antitoxin, and that it is advisable to have as high a concentration of antitoxin as possible in the fluids surrounding poisoned cells.

This view of the action of the antitoxin gives more encouragement to the physician to persevere vigorously with serum treatment. It emphasizes the advisability of employing very large doses of serum so as to saturate the system with antitoxin, and thus not only neutralize any toxin which may be passing from the focus of infection into the blood, but also to extract toxin from cells into which it has already passed.

Such treatment, suggested by the results of experimental research, is practically identical with that employed by many physicians to-day as the outcome of years of bedside observation.

Ernest E. Irons (1912) analysed 252 cases collected by Anders and Morgan* and classified them. The incubation periods of the fatal and non-fatal cases showed practically the same relation. His figures are:—

---

* *Journ. Amer. Med. Assoc*, July 29, 1905, p. 314.

			Mortality.
Total number of cases	254	...	71 per cent.
Cases treated without serum	142	...	77 ,,
Cases treated with serum	112	...	63 ,,
Cases treated with small amounts of serum	71	...	70·4 ,,
Cases treated with large amounts (100 c.c. or more) of serum ...	41	...	51·0 ,,

If we compare the mortality of all the cases treated with serum with that of the cases treated without we must allow that the use of serum brings little if any advantage. But if we compare the mortality in cases treated *with large amounts of serum* with the mortality of the cases treated *without serum*, then the beneficial results following such use of serum become manifest.

W. H. Park (1910) says that when a large intravenous dose is given within a few hours of the onset of the symptoms the effect is marked. More than 50 per cent. of the patients so treated recovered, "some of whom I feel perfectly sure would have died without the serum." At the first sign of actual tetanus 10,000 to 20,000 U.S.A. units should be given intravenously, and followed every twelve hours by further injections. The later injections may be given subcutaneously if the intravenous route becomes difficult. Torres (1912), after an experience of 110 cases of acute tetanus in eight years with a mortality of 32·7 per cent., gives an intravenous injection of 120 c.c. of serum as the rule. He repeats it twice, or even oftener, in the first twenty-four hours if necessary, and then gives 100 c.c. daily if the symptoms are still present.

Penna (1913) also gives injections of 100 c.c. intravenously once or twice in the twenty-four hours, and keeps it up for several days *even though the patient may be improving*.

Van der Bogert (1913) cites:—

(1) Strock (1907), who treated his cases of tetanus during six years with small doses of serum and had a mortality of 100 per cent. Then he treated five cases with very large doses, and the mortality was 20 per cent.

(2) The three cases of Young (1912), which appeared hopeless, but recovered—a boy had 150,000 U.S.A. units, a man had 220,000 U.S.A. units, and a girl aged 14 had 587,000 U.S.A. units.

Many other similar records could be quoted, if space permitted, to show that among those who not infrequently meet with cases

of tetanus the tendency of late years has been to use much larger doses of antitoxin than formerly, and that the use of these large doses seems to be followed by more uniformly beneficial results than were observed in former years when only small doses were employed.

Modes of Administration.

Besides the size of the dose the mode of administration of the serum has an influence upon the result. Serum may be given:—

(1) Intracerebrally.
(2) Subarachnoidally.
(3) Intraneurally.
(4) Intravenously.
(5) Intramuscularly.
(6) Subcutaneously.

(1) Intracerebral injections have given very good results in animals, and in several cases in man also, but the risk of permanent injury to the nervous system has prevented this method coming into general use. Ballance (1914), however, suggests that the introduction of serum into the lateral ventricle might be used in tetanus, as he thinks that with reasonable care the operation as a whole is free from danger.

(3) Intraneural injections were strongly recommended by Rogers (1905), but they are not free from risk, and are seldom used.

(4, 5 and 6) As regards the intravenous, intramuscular, and subcutaneous route the final result is the same in all three. The only difference is in the time taken for the antitoxin to be absorbed and distributed throughout the body. In the case of the intravenous method it is a question of a few minutes: of the intramuscular, of a few hours; while after subcutaneous injections it is one to two days before the maximum concentration of antitoxin in the blood is reached.

There remains the subarachnoidal route to consider.

Descos and Barthélemy (1902) experimentally showed that intraspinal injections gave the best result.

Von Graff (1912) carried out a number of experiments in the Serotherapeutic Institute in Vienna, and came to the conclusion that this route was the most effective, and that next to it came the intravenous.

Permin (*loc. cit.*) considers that intraspinal are just as good as intraneural, and are better than intravenous, inoculations.

W. H. Park (1914, personal communication) has treated six successive cases of tetanus by intraspinal injections, and all have recovered.

Hofman (1907) states that of thirteen cases which had serum beneath the skin 53·8 per cent. died, whereas of sixteen cases which had serum subdurally only 12·5 per cent. died, and these sixteen cases included a number of extremely severe cases with brief incubation periods. He recommends that the intraspinal injections should be given every two to three days and the subcutaneous daily. Graser (1910) also advises serum by intralumbar injection every two to three days and daily beneath the skin. Gobiet (1904), Neugebauer (1905), Jerie (1908), and Buffagni (1910) and others speak of the good effect of intraspinal injections of antitoxin, and Buffagni says:—

(1) After the first injection one observes an increase in the symptoms, reaching a maximum in forty-five hours, and then passing off and giving place to improvement.

(2) The organization of the patient reacts to each injection of tetanus antitoxin by a rise in temperature of 1·5° to 2° C., which passes off in ten to twelve hours.

(3) After each injection more or less distinct improvement of all conditions occurs, and especially of the tetanic attacks.*

The method of procedure in the serum treatment of a case of tetanus would then be somewhat as follows:—

(1) The injection beneath the arachnoid, or in very severe cases even (Ballance, 1914) into the lateral ventricle, of as large a dose of antitoxin as may be conveniently given—for example, 3,000 to 8,000 U.S.A. units.

(2) The injection into a vein of a large dose—9,000 to 16,000 U.S.A. units—with the object of flooding the system with antitoxin as soon as possible.

(3) The injection of antitoxin intramuscularly; and

(4) The repeated injection of antitoxin subcutaneously—both with a view of keeping up the concentration in the blood.

Clinical experience, both in man and horse, has shown that it is absolutely necessary to continue the injections, even though improvement has apparently set in, as otherwise the symptoms are

* These observations of Buffagni are very like those made by some physicians with regard to intraspinal injections of antimeningococcic serum.

very liable to return—in some cases with greater intensity than at first.

"Idiopathic" Tetanus.

The absence of any history of injury sometimes makes the diagnosis of tetanus at first very difficult. In the past such cases were classed as rheumatic or idiopathic tetanus, but we know now that for tetanus to declare itself the tetanus bacillus must somehow have gained entry into the body.

It has been shown experimentally that tetanus spores free from toxin or foreign material may be injected into animals without causing tetanus, and that they can become disseminated in the body and remain latent for a time. Then if suitable conditions arise, such as the formation of a necrotic area in the tissues, such latent spores may germinate and give rise to tetanus.

Canfora (1907) infected animals subcutaneously with tetanus bacilli and found that they spread all over the body. He also injected toxin-free tetanus spores, and found them in the blood twelve hours later. They may remain in the blood for ten to fifteen days, during which time very slight injuries are sufficient to set up tetanus. Later the spores become localized in the liver, spleen, lungs, kidneys, lymph glands and marrow, where they may remain latent for some months.

Semple (1911) came to the conclusion that an injection of a solution of quinine might cause enough destruction of tissue to produce conditions favourable for the germination of spores.

It behoves us, therefore, to bear tetanus in mind, even though there be no history of injury, whenever we meet with symptoms similar to the premonitory symptoms mentioned by Evler and found to be present in so many cases of this disease.

Preservatives in Serum.

Most serums have a small amount of preservative (phenol, trikresol, chloroform) added to them, and when doses such as 120 c.c. are given at one time, the presence of preservatives requires consideration and raises the question as to how much preservative can be given without ill-effect.

Baccelli (1911), who strongly recommends that tetanus should be treated with subcutaneous injections of carbolic acid, states that not less than 1 gramme should be given daily; J. H. Haberlin

(1913) in a case of hydrophobia gave 22½ gr. of phenol subcutaneously in twelve hours without any evidence, either locally or generally, of any deleterious effects; Natoli (1899) injected 5·25 grammes of phenol subcutaneously in eighteen days; and Ascoli (1898) gave 75 c.c. of a 3 per cent. solution without any subsequent toxic symptoms.

The probability of ill-effects being due to the preservation in serum when administered intrathecally has been fully discussed and negatived by Flexner in the case of autoemeningococcic serum. It may, then, be safely assumed that the amount of phenol put into serum is not likely to have any serious consequences.

Conclusions.

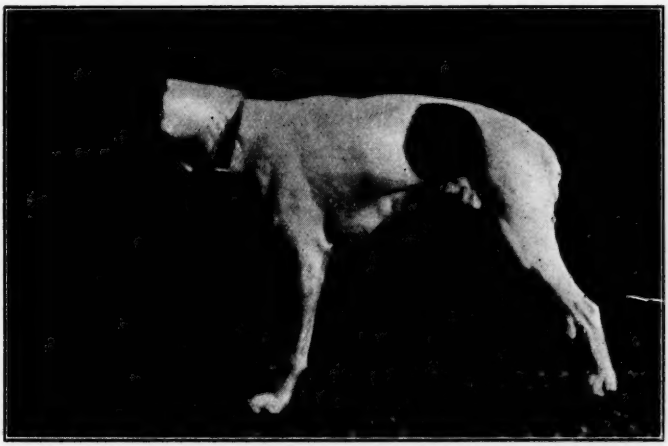
Tetanus may be cured by the administration of antitoxin, provided that the serum treatment is begun early in the attack and is pursued vigorously and continuously. Unfortunately, in the present state of our knowledge a diagnosis is as a rule made only when the disease is in a stage so advanced as to make the results of treatment uncertain, even though very large doses of antitoxin are used. These large doses are costly, and place the serum treatment of tetanus practically out of the reach of those with shallow purses—unless, of course, the serum be provided by the State. But in the prophylactic use of serum there is within the reach of everyone a means of checking the disease. It has been proved beyond the shadow of a doubt that wherever the prophylactic use of antitoxin has been carried out systematically tetanus may be said to have disappeared. Tetanus should therefore be looked upon as a preventible disease, and, when one realizes this, there flashes across the mind the memorable question, "If preventible, why not prevented?"

BIBLIOGRAPHY.

Ascoli, 1898. *Bull. della R. Academ. Medic. d. Roma.*
Anders and Morgan, 1905. *Journ. Amer. Med. Assoc.*, 29, vii, p. 314.
Brandenstein, 1908. *Deutsch. Zeitschr. f. Chir.*, Leipzig, xcii.; Abs. *Journ. Amer. Med. Assoc.*, 1908, p. 1386.
Bockenheimer, 1909. *Deutsch. med. Woch.*, p. 44.
Baccelli, 1911. *Berl. klin. Woch.*, p. 1021; *Centralbl. f. Bakt.*, 1912, I, Ref. 51, 413.
Buffagni, 1910. *Clinic. Med. Ital.*, 1910, 299; *Centralbl. f. Bakt.*, I, Ref., 1911, 48, 254.
Ballance, 1914. *Lancet*, i, 1525.
Canfora, 1907. *Centralbl. f. Bakt.*, I, Orig., 45, p. 295.
Choukévitch, 1911. *Ann. Inst. Pasteur*, xxv, p. 351,
Cernovodeanu and Henri, 1907. *Compt. Rend. Soc. Biol.*, 62, 812.

DESCOS and BARTHÉLEMY, 1902. *Compt. Rend. Soc. Biol.*, 1055 and 1057.
DOLLY, 1908. *Journ. El. Mitchell Sci. Soc.*, 1908, xxiv, 23; *Centralbl. f. Bakt.*, 1910, I, Ref., 46, 290.
DIEUDONNÉ, 1909. *Recueil Méd. Vét.*, 1909, 433; *Bull. Inst. Past.*, 1909, 855.
EVLER, 1910. *Deutsch. med. Woch.*, 1910, 961; *Berl. klin. Woch.* xlvii; Abs. *Journ. Amer. Med. Assoc.*, 1910, October, 1507.
VON GRAFF and MENSCHIKOFF, 1912. *Centralbl. f. Bakt.*, I, Orig., 61, 226.
GOBIET, 1904. *Wien. klin. Woch.*, 1904, xvii, 1256; *Bull. Inst. Past.*, 1905, iii, 93.
VON GRAFF, 1912. *Mitteil. a. d. Grenzgeb. d. Med. und Chir.*, xxv, 145; Abs. *Journ. Amer. Med. Assoc.*, 1912, October, 1414; *Centralbl. f. Bakt.*, I, 1912, Ref. 55, 171.
GRASER, 1910. *Deutsch. med. Woch.*, 1910, 1503; *Centralbl. f. Bakt.*, I, 1911, Ref. 48, 251.
J. H. HABERLIN, 1913. *New York State Journ. of Medicine*, xiii, September; Abs. *Journ. Amer. Med. Assoc.*, 1913, October 18, p. 1488.
HOFMAN, 1907. *Beitr. z. klin. Chir.*, Tübingen, lv, October; Abs. *Journ. Amer. Med. Assoc.*, 1908, January, 160.
HUGUIER, 1909. *Recueil Méd. Vét.*, 1909, 356; *Bull. Inst. Past.*, 1909, 855.
IRONS, E. E., 1912. *Journ. Amer. Med. Assoc.*, December 7, 2084.
JOSEPH, 1910. *Zeitsch. f. Infektkr. u. Hyg. d. Haustier*, 1910, vii, 96; *Bull. Inst. Fast.*, 1910, p. 803.
JERIE, 1908. *Mitteil. a. d. Grenzgeb. d. Med. u. Chir.*, xix; *Centralbl. f. Bakt.*, 1909, I, Ref. 43, 765.
KRAUS and AMIRADZIBI, 1910. *Zeitsch. f. Immunitätsforscht.*, I, Orig., vi, p. 1.
KITASATO, 1890. *Zeitsch. f. Hyg.*, x, 267.
VON LINGELSHEIM, 1913. *Handb. d. Path. Micro-organ.*, Kolle and Wassermann, 1913, iv, 737.
LUKAS, 1914. *Zeitsch. f. Tiermel.*, 1914, 18, 17; *Centralbl. f. Bakt.*, I, Ref. 61, 394.
MOHLER and EICHHORN, 1911. 28th Annual Report of the Bureau of Animal Industry, 1911.
MCCLINTOCK and HUTCHINGS, 1913. *Journ. Inf. Dis.*, xiii, 309.
NATOLI, 1899. *Gaz. degli Osped. e del. Clinic.*
NEUGEBAUER, 1905. *Wien. klin. Woch.*, xviii, 449; *Bull. Inst. Past*, iii, 580.
PARK and WILLIAMS. *Pathogenic Bact. and Protoz., New York*, 1910, p. 243.
W. H. PARK, 1910. *Journ. Amer. Med. Assoc.*, 1910, January 22, p. 254.
PERMIN, 1913. "Commun. de l'Instit. Serother. de l'État Danois," viii.
PARKER HITCHENS, 1910. *Amer. Veterin. Review*, xxxvii, 597.
PENNA, 1913. *Semana Med.* (Buenos Ayres), xx, October 16; Abs. *Journ. Amer. Med. Assoc.*, 1914, January, 249.
RÖMER, 1909. *Zeitsch. f. Immunitätsfor.*, 1909, I, Orig. I, 363.
RABINOWITSCH, 1907. *Arch. f. Hyg.*, 1907, lxi, 103; cited, *Journ. Amer. Med. Assoc.*, 1908, 933.
ROGERS, 1905. *Journ. Amer. Med. Assoc.*, July 5, p. 12.
SOLIERI, 1910. *Centralbl. f. Bakt.*, I, Orig., 55, 141.
SIMON, 1909. *Münch. med. Woch.*, p. 2264.
SIMON, 1913. *Infection and Immunity*, London, 1913, p. 236.
F. R. TORRES, 1912. *Semana Med.* (Buenos Ayres), xix, No. 39; Abs. *Journ. Amer. Med. Assoc.*, November 30, 2014.
TAROZZI, 1905. *Centralbl. f Bakt.*, I, Orig., 40, pp. 305 and 451.
VAILLARD, 1912. *Médicaments microbiens*, Paris, 1912.
VAN DER BOGERT, 1913. *Journ. Amer. Med. Assoc.*, February 1, p. 363.

Clinical Article.



A Case of Tetanus in a Dog.

[This photograph should have been inserted in the Clinical Article by Mr. T. M. Inglis, M.R.C.V.S., of Forfar, on p. 518 of the October issue.]

SUBCUTANEOUS TUBERCULOSIS IN A COW.

By CH. PERARD.

Public Health Veterinary Surgeon of Seine.

On examining a Normandy cow 15 years old, discarded from a dairy and affected with pulmonary tuberculosis, some changes were noted at the level of the middle region of the left face of the neck.

These lesions, which consisted of small irregularly bosselated tumours from the size of a grain of millet seed to that of a lentil, isolated or aggregated in small groups, were situated in the subcutaneous connective tissue in the thickness of which they formed plastron of about 15 cm. in diameter and ½ cm. to 1 cm. in thickness.

Some of them were adherent to the internal face of the skin, others to the external face of the superficial muscles, as is evident from the fact that a large number of them have been divided by the

butcher's knife during the operation of skinning. On section they were of yellow colour and fibrous consistence ; a certain number of them showed commencing calcification. The neighbouring lymphatic ganglions showed no sign of tuberculosis. These subcutaneous lesions were quite different from those already recorded by Ramon and myself, which resemble, to a certain extent, those seen by Darier and Roussy.

They are not to be compared : in one case nodules round or oval surrounded by a fibrous shell of the size of a filbert nut, of elastic consistence, and composed of a homogeneous substance of greyish tint ; in the other, little hard tumours, bosselated, fibrous or partially calcified, and of a beautiful yellow colour. The fact that the cadaver presented besides unequivocal signs of tuberculosis made these subcutaneous alterations particularly suspicious ; attempts to find the tubercle bacillus failed. Two guinea-pigs inoculated subcutaneously with the crushed product of these lesions died in fifty-three and fifty-eight days ; the autopsy showed that they had succumbed to tuberculous infection.

It is curious to note that on sale of the animal, the purchaser some months previously had tested her with tuberculin on the left side of the neck. Was there any connection between this injection and the lesions found in this region at the autopsy ?—*L'Hygiène de la Viande et du Lait.*

VICTORIA VETERINARY BENEVOLENT FUND.

THE quarterly meeting of the Council of the Victoria Veterinary Benevolent Fund was held at 10, Red Lion Square, London, on Thursday, October 8, 1914. There were present: Mr. S. H. Slocock (in the chair), Sir John M'Fadyean, Sir Stewart Stockman; Messrs. F. H. Gooch, Walter Burt, W. Freeman Barrett, S. Villar, H. A. MacCormack, G. A. Banham, N. Almond, R. C. Trigger, Professor Wooldridge, and W. Shipley (Hon. Secretary).

Letters of apology were received from Messrs. J. Dunstan, F. Hobday, P. J. Simpson, and E. Alfred West.

The minutes of the previous meeting having been confirmed, the Secretary presented his quarterly report.

The SECRETARY (Mr. William Shipley) said: "It is important that I should present an interim report on our financial position.

At present we have overspent our income by £17 7s. 3d., having a debit balance at the bank of £11 14s. 4d. We have to meet liabilities in grants already agreed to, to Christmas next, the sum of £75 18s. I anticipate a further expenditure of £30 for passages and outstanding accounts, and one is well aware that it is a practical impossibility to realize any securities for some time to meet these commitments. As against this we have outstanding subscriptions and possible renewals of donations, as per last year, the sum of £54, many, of course, which have not been paid owing to the fact that many helpers are engaged on military duties, and others have had their incomes temporarily reduced owing to the war. I estimate the income from these sources will not produce more than £27. This is a generous estimate. I sincerely hope that every endeavour will be made to induce those members of the profession who are following the even tenor of their way to step in and fill the gap. Our income from investments will be £32 16s. This will leave us with a deficit of £63 9s. 3d. at the end of the year. Of course, I would advise you to bear in mind that the probability of further applications for help must arise, and it will occur to us all that we should be prepared to meet this distress most liberally. Let the members of the profession who are leaving their homes and country for the defence of what is right and just feel that their brother practitioners are doing their best for the little ones left behind. I apprehend a serious financial condition soon or at the end of the year—a reduced subscription list and increased appeal for help."

The grants to the old recipients were considered fully. On the proposition of Mr. N. ALMOND, seconded by Mr. H. A. MACCORMACK, it was decided to pay arrears in grants to Mrs. M. C. Timms, and continue the same until some more definite evidence has been obtained.

It was decided that no further action could be taken in re-considering the grant to Miss Worsley unless further evidence can be produced.

After a long consideration of the application of Mrs. Farr, of Cullompton, Devon, it was proposed by Sir JOHN M'FADYEAN, and seconded by Mr. GOOCH, that temporary assistance be given at the rate of 10s. per week, instructions being given to the Secretary to make every endeavour to take some action with the

view of getting the two children elected to some charitable school. Failing any such institutions in the West of England, endeavours should be made to obtain the election of these children into the London Orphan Asylum.

Serious consideration was given to the financial report and expressions that every effort should be made to induce new members to take the place of those engaged on military duties and to make provision for any further cases which might occur before the end of the financial year.

A vote of thanks to the Chairman concluded the business of the meeting.

Translation.

SUCCESSFUL CAMPAIGN AGAINST THE GADFLY PLAGUE OF CATTLE.

Towards the end of February the gadfly plague makes itself evident by reason of the appearance of the lumps on the backs of cattle in which the larvæ of the fly are situated. Not merely do the skins of the animals suffer, but the milk-giving capacity of the cows declines. According to the statistics of the Committee for the Suppression of the Plague in Berlin the loss of value in the skin of an affected beast is 4 to 5 marks, and since one-fourth of the dressed hides in Germany is injured by larvæ holes the yearly loss on the total number of skins is from four to five million marks.

In Denmark in isolated instances it has been noticed that, after pressing out of the warbles, cows have given five litres more milk daily than previously. Although milking cows are not so numerously affected with warbles as other cattle, yet the loss in milk-giving capacity of cows that are warbled must amount in Germany to many million marks. We are not powerless against the complaint. By a planned campaign whole districts, if not entirely freed from the trouble, may be rendered almost free from it.

This annihilation of the plague has been the object of "the Committee for the Campaign against the Gadfly in Berlin." Investigations into the life conditions of the fly, and the transference of its eggs to cattle, have made great advance and have given much impulse to the fight against the scourge. At the last sitting of the Committee Dr. Gläser gave an account of his experiments in the year 1913. A test with ten heifers of equal age, all affected with warbles, showed that five of them, after being freed from the larvæ, gained 34 lb. more in weight in a given period than the other five that were left alone. This corresponds at to-day's price to a difference of 15 to 16 marks per head in favour of the warble-free animals. The great warble-killing trials in the circle of Neuhaus which the Committee conducted led to the destruction of 46,231 larvæ. The cost amounted to 419·33 marks and each removed larva cost

0·906 pfennigs for removal. In one district an expert worker in 83½ hours' work removed 12,253 larvæ at a cost of 0·40 marks. If one estimates the injury per cow from the above figures at 15 to 16 marks during May to October, then one can only urgently advise cattle owners to have their animals treated.

The freeing of the animals from warbles commences by ridding all the cattle in the cowhouse or shed from all accessible larvæ. In the German leaflet the following procedure is advocated: The larvæ in the largest lumps are endeavoured to be got rid of by pressure with the fingers. If this, on account of insufficient development of the parasite, does not succeed it is recommended to introduce a strong needle into the small opening in the skin and to impale the larva whose black hind end may generally be seen just behind the aperture; the contents of the larva then runs away. By powerful pressure of the fingers one now seeks to empty the warble lump. The irremovable impaled larva dies and gradually sloughs away. Injury to the health of the cow is not to be feared. Whilst at pasture an examination of the cows must be made at intervals of fourteen days. By so doing larvæ developing later on may be removed as heretofore. Larvæ removed on meadow land must be destroyed. Killing the larvæ by smearing, previous to driving the cattle out, has been tried. Very good success has been achieved by the use of birch tar oil, of which a kilogram only costs 75 pfennigs. These experiments are being continued this spring.—G. M.—*Oesterreichische Woch. für Tierheilkunde.*

Reviews.

The Agricultural Journal of the Union of South Africa, August, 1914. Edited by H. J. Choles, F.S.S. Issued by the Agricultural Department. Published at Pretoria.

The Editor calls attention to the importance of the insurance of live stock, and announces the founding of the Farmers' Horse and Mule Insurance Association. He discusses pig insurance as practised in England and Wales, and advocates similar measures with farm live stock in South Africa.

Mr. H. W. Taylor has an interesting and valuable article on "Cotton: How to Make it of Economic Importance to South Africa." Several of the illustrations to his paper show the operations of the Rustenburg Tobacco and Cotton Experimental Station, and apparently the growing of cotton might be profitably carried on in selected regions of South Africa. An estimate given by Mr. Taylor is that out of a world population of 1,500,000,000, about 500,000,000 regularly wear clothes, 750,000,000 are partially clothed, and 250,000,000 go naked. At the present time the world's production of cotton is about 20,000,000 bales, or about one-half enough to clothe the population of the entire globe. New and productive cotton-growing areas are necessary, and the claims of South Africa need consideration.

Mr. D. Hutcheon, M.R.C.V.S., writes on "Lung Sickness in Cattle" and "Bots or Paapjes." In reference to the preventive treatment for the latter, Mr. Hutcheon mentions dressing the skin to keep off the flies and removal of the eggs by frequent careful grooming. The singeing or painter's lamp is a quicker and more effective way of removing the eggs than careful grooming, but in many parts of South Africa perhaps this lamp is unknown.

Mr. Reinecke, B.A., deals instructively with "Lime and the Liming of Land."

The journal concludes with rural notes, the new scab regulations, and correspondence. The periodical must be doing excellent work among the agricultural community, and the farmer who reads will find in it a real friend. G. M.

The Rhodesia Agricultural Journal, June, 1914. Edited by the Director of Agriculture, assisted by the Staff of the Agricultural Department. Published bi-monthly. Price 5s. per annum. Printed by the Argus Printing and Publishing Company, Ltd., Salisbury, Rhodesia.

This well got up and clearly printed periodical touches on all matters of importance and interest to Rhodesian agriculturists and colonists. Mention is made of the record crop of tobacco that has been grown in the State, amounting approximately to 2,240,000 lb. A new society, called the Rhodesian Tobacco Planters' Co-operative Society has been formed to further the growth of the plant, and it is hoped that buyers will eventually come forward in goodly numbers to take up the supply and encourage the industry.

The first maize-reaper and binder has been at work in the country. It was drawn by six oxen and did its work satisfactorily.

Friesland cattle and merino sheep, which both appear to do well in the colony, have been procured from Germany. There are 370 tanks in existence in the country for dipping cattle as a preventive of infection from tick-borne diseases. The demand for these commodities is still great, and no other single preventive measure can compare with this precaution against many ailments.

Mr. R. McIlwaine, M.A., LL.B., has an instructive article on citrus-growing. His experiments have chiefly been conducted with oranges, tangerines and grape-fruit, and he writes that he is "quite satisfied that the country is exceptionally fitted for citrus-growing." An export trade must be built up, and, as the trees require unremitting attention, "ten trees well looked after are more profitable than one hundred neglected."

Mr. B. Rosenthal writes on "How to Cure Hides and Skins," and his directions are short and concise. The *hides* of cows and oxen are either salted or wind-dried, but wind-drying cannot be used to cure the *skins* of sheep and goats.

Mr. Ll. E. W. Bevan, M.R.C.V.S., has a "Note on the Treatment of Biliary Fever of the Horse with Trypan Blue." He comes to the conclusion that the drug is useless in the complaint. Chief Veterinary Surgeon J. M. Sinclair furnishes veterinary reports for March and April, from which it would seem that not much coast fever is rife in

the districts at present, and all imported horses, mules and donkeys that were tested with mallein were found free from glanders. Veterinary lectures are delivered to farmers, and many useful bulletins on agriculture, crops, entomology, veterinary matters, &c., may be obtained free of charge from the Department of Agriculture. The periodical is well illustrated and a credit to the compilers and printers. G. M.

Disinfectants and Disinfection. By Walter Jowett, F.R.C.V.S., D.V.H. (Veterinary Division), Department of Agriculture, Cape Town. Government Printing and Stationery Office, Pretoria.

This is a reprint in pamphlet form from the *Agricultural Journal of the Union of South Africa*, intended to enlighten animal owners with respect to disinfectants and disinfection in regard to the buildings and objects of contact rendered infective by animals suffering from dangerous communicable diseases. Cremation is discussed and Major-General Smith's device for incinerating carcases described.

Physical means of disinfection comprise burning, moist heat and steam. Chemical disinfectants include gaseous agents such as sulphur dioxide gas, chlorine, and formaldehyde. The chemical solutions recommended by the author are phenol, crude carbolic acid, cresol, corrosive sublimate, formalin, and chlorinated lime. Routine disinfection, disinfection of hides and skins, disinfection of attendants, and methods of preparing whitewash conclude the pamphlet. There is no doubt that there is great need of putting a plain system of disinfection before animal owners and attendants, and, doubtless, Mr. Jowett has done excellent service by getting his paper circulated in pamphlet form. Headwork is needed in the case of effective disinfection not less than in the more intricate problem of the therapy of disease. There is much ignorance rampant as to what constitutes thorough disinfection, and a plentiful sprinkling of germicides or an abundant swilling with liquid disinfectants may mean zeal, but unless done intelligently is only misapplied effort. Probably there is a greater need for education in South Africa on the subject of Mr. Jowett's pamphlet than there is here, but knowing men recognize the great necessity there is for enlightenment of the laity on this subject here. Mr. Jowett's pamphlet cannot help but be one of the most useful ever issued by the Department of Agriculture of South Africa.

G. M.

Eighteenth Annual Report of the New York Zoological Society chartered in 1895. Objects of the Society : A Public Zoological Park ; the Preservation of Native Animals and the Promotion of Zoology. 1913. Office of the Society, 11, Wall Street, New York. Printed by Clark and Fritts, 209, West 38th Street, New York.

This is an enlightening record of reports of the various departments of animal life in the New York Zoo. There are twelve full-page illustrations in the work, all being excellently produced, and perhaps the most interesting being those of the landing and shipment of

porpoises from Cape Hatteras to the Aquarium of the Zoo. Two attempts were made to obtain live porpoises for the large central pool of the Aquarium. The first consignment died during and after transference by reason of being forwarded dry to their destination. The second lot were put in tanks with water at the temperature of that of Cape Hatteras, and they are now doing well in the large pool of the gardens which is 7 ft. deep and 37 ft. in diameter. They are the only porpoises in captivity, and within recent months they have given evidence that they will breed in such quarters. The Report of the Veterinarian and Pathologist to the Society, Mr. W. Reid Blair, D.V.S., shows that tuberculosis has chiefly been confined to the primates, and that the type is always human, whilst that of the carnivores is of the bovine type. Gastro-enteritis affected a good many of the hoofed animals, and was due to irritating substances in clover and alfalfa. Mouldy hay and grain causing fungi poisoning chiefly in deer were responsible for several deaths. Pneumonia affected both primates and small mammals, and parasitic diseases and rickets were both in evidence. An unusually large number of animals met violent deaths as a result of fighting with cage or corral mates.

The finance and membership of the Society seem to be in a flourishing state, and that the place is appreciated is shown by the fact that in 1913 there was an increase of nearly a quarter of a million in the attendance of the public and that the record figure of 1,943,683 persons was reached.

We are indebted for the Report to Mr. Gilbert Congdon Wood, one of the Members of the Society, and we take the opportunity of thanking him for it here. G. M.

Lehrbuch der Topographischen Anatomie des Pferdes (Text-book of the Topographical Anatomy of the Horse). By W. Ellenberger, M.D., Ph.D. and D.V.M., and H. Baum, Ph.D., Professors at the Dresden Veterinary College. Price 22 marks. Two hundred and fifteen figs. in the text, many of which are coloured. Pp. 427. 1914. Publishers : Paul Parey, Hedemannstrasse, Berlin.

This text-book has been brought out chiefly for the use of students and to replace in shorter and handier form a three-volume work issued on the same subject in 1897. The text of the bulkier volumes has been considerably shortened, but the number of the illustrations remains the same.

The anatomical relationship of different structures in the horse's body is lucidly described and illustrated, and to the surgeon and anatomist the work will be very helpful. From college teaching one is apt to look on the various tissues as distinct and apart from each other and to forget the intimate relationship between them and the interdependence of each on all and all on each. It is in books like the one under review that these isolated views get corrected and remedied, and the everyday routine of practice soon makes one grateful for a good anatomical text-book showing the relationship of varied parts. The various regions of the body, such

as head, neck, thorax, abdomen, &c., are taken in order, and every tissue of which they are composed, from the largest to the most minute, comes under review. The illustrations are a strong feature of the work and are admirable in every respect, and the method of executing the drawings of different tissues, so that each may be recognized distinctly by the student at a glance, is very commendable.

The work is bound and printed in the best Paul Parey style, and we feel sure that it will circulate far beyond its place of origin in Germany.

We have no book exactly like it in this country, and any author who intends producing such a handy work here cannot do better than take Ellenberger and Baum's volume as his model. G. M.

Annual Report of the Bengal Veterinary College and of the Civil Veterinary Department, Bengal, for the year 1912-13. Published by the Bengal Secretarial Book Depot, 1913. Price 9d.

Major A. Smith reports that when he took over formal charge of the Bengal Veterinary College on June 4 there were 107 students in the three classes A, B, and C. At the examinations in March 72 students passed, and 22 of these received their diplomas. 2,428 patients were treated at the College during the year. A new hospital for dogs has been erected, and some of the College buildings have been improved. Twenty-nine horses were tested for glanders in the Contagious Diseases Hospital, 5 were destroyed for glanders, 1 died of the disease, 21 were discharged as free, and 1 remained under observation. Rinderpest, foot-and-mouth disease and tuberculosis were dealt with by the Department. The Raymond Research Laboratory did useful work during the year in the investigation of the prevalent specific diseases. The British Commission on Foot-and-Mouth Disease was supplied with a large amount of material for its work by the laboratory.

Mr. P. J. Kerr, M.R.C.V.S., Superintendent of the Civil Veterinary Department in Bengal, furnishes his Annual Report. As in the case of many veterinary surgeons working for the Government in India, he seems to have had an immense amount of work to do. During a period of five months he travelled 5,733 miles by rail, 907 by steamer, and 279 by road. He inspected many farms and districts, provisionally selected seven sites for Dacca New Veterinary Hospital, and attended two outbreaks of glanders. An inspector from the Department was trained at the Bengal College, and three reserve veterinary assistants also attended courses.

Of the fifty-five assistants employed by the Department, eighteen were stationary and thirty-five itinerant. They all worked fairly well, but showed lack of keenness. Cattle poisoning is common in the district, and it seems almost impossible to detect the culprits. The establishment of a cattle farm is urgently needed in the district, the people knowing literally nothing about breeding. Small demonstration farms might help to eradicate the native indifference in this matter. There is great need for a second

European Superintendent in the province, the present Superintendent being much overworked, and additional veterinary assistants are required and could all be fully and usefully employed. Lack of funds, however, militates against progress. Foot-and-mouth disease, rinderpest, hæmorrhagic septicæmia, and anthrax were the chief diseases investigated by the Department, and protective inoculation was followed by immunity in nearly all cases. Science is evidently improving animal matters in Bengal, but the co-operation of the officers of other Government departments and of the inhabitants generally is needed to bring about a greater measure of success. G. M.

ITEMS OF WAR NEWS.

It is pleasing to the profession to read of the recognition in dispatches of some of its members, and we congratulate most heartily the following officers whose names were mentioned by General French in his report: Captain W. I. Macauley, Captain Oliver, Captain F. W. Pawlett (T.F.), Lieut.-Colonel W. D. Smith, Captain E. J. Wadley.

An extract, too, from a letter sent by Lieutenant T. Davies, M.R.C.V.S., to a friend in England shows that the veterinary officer sometimes comes in for a very warm time, as, indeed, has already been shown by the deaths of those whose names have already been added to the "Roll of Honour" of men who have given their lives for their country:—

"As —— is now pretty old war news I may mention a little about it.

"It was on September 1, and we were billeted in the village. About 5.30 a.m. the Germans attacked with 15 guns, maxim guns and rifles in great force, at close range. We were off saddle, and Colonel Ansell and I were having breakfast in a farm. We all ran to the horses and saddled up amidst a hail of bullets and shells, and Colonel Ansell took the regiment to a flank, and with other units helped to capture 10 of the guns, kill a lot of Germans, and take about 40 prisoners.

"Colonel Ansell was killed, De Crespigny of the Bays, and nearly all the officers of L Battery R.H.A. were killed or wounded. I had my horse shot under me, but I got off without being touched. It was very exciting."

NOTE.—All communications should be addressed to 8, Henrietta Street Covent Garden, London, W.C. Telephone, 4646 Gerrard. Telegrams, "Baillière, London."

Letters for the JOURNAL, literary contributions, reports, notices, books for review, exchanges, new instruments or materials, and all matter for publication (except advertisements) should be addressed to the Editors.

Manuscript—preferably typewritten—should be on one side only of paper, marked with full name of author.

Illustrations for reproduction should be in good black or dark brown on white paper or card.

Advertisements and all business matters relating to the JOURNAL should be addressed to the publishers, Messrs. Baillière, Tindall and Cox.